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EDITORIAL

METRONIDAZOLE AND *TREPONEMA PALLIDUM*

Metronidazole, after penicillin, is probably the drug most commonly used in the treatment of patients suffering from genital infections. It is known to be effective not only against *Trichomonas vaginalis* but also against the organisms of Vincent's infection, which include a spirochaetal component. In consequence there has been some anxiety as to the possibility that it may affect *Treponema pallidum* and perhaps suppress the signs of early syphilis without curing the disease. This matter was considered by Scott-Gray and Murrell (1961), who found, however, that a short course of metronidazole, amounting to 1·8 g. in 48 hours, appeared to have no effect in a case of primary syphilis. Davies, McFadzean, and Squires (1964) reported that the minimal inhibitory concentration of metronidazole for the cultivable Reiter treponeme, which appears to be closely related to pathogenic *Treponema pallidum*, was as low as 0·02 μg./ml. Yobs, Clark, and Schroeter (1966) found that relatively large doses of metronidazole had no effect on the course of syphilis in rabbits infected with the same organism. As reported on p. 197, Davies has investigated the effects of this preparation in the treatment of patients with early syphilis. He found that doses of 2 to 4 g. daily given for periods of 5 to 9 days caused the disappearance of *Treponema pallidum* from the lesions of six patients suffering from secondary syphilis within 3 to 8 days after the commencement of treatment, and that the lesions subsequently healed. These doses are, of course, much in excess of those commonly used for the treatment of trichomoniasis which usually amount to 600 mg. daily. Davies measured the concentrations of metronidazole in the sera of three of his patients and found that levels rose to 44·1, 61·5, and 72·5 μg./ml. respectively. In one case the level in the cerebrospinal fluid was determined and amounted to 80·4 μg./ml. Wilkinson, Rodin, McFadzean, and Squires (p. 201) describe the results of estimations of metronidazole in the blood of twenty female patients suffering from trichomoniasis who received standard dosage, namely 600 mg. of the drug daily for 7 days. Estimates made toward the end of the course of the treatment showed serum concentrations varying from 1·0 to 20·5 μg./ml., but with one exception all were below 10 μg./ml. None of the patients had clinical or serological evidence of syphilis. In tests against the Nichols strain of *Treponema pallidum* it was found in four experiments that the concentration of metronidazole producing 50 per cent. immobilization of treponemes was 3·6, 3·6, 4·1, and 9·5 μg./ml. Undiluted serum from eight of the patients immobilized 50 per cent. or more of the treponemes, and in six of these the content of the sera was 5·0 μg./ml. or more by polarography. They admitted to hospital one patient suffering from primary syphilis and treated him with metronidazole by mouth, 200 mg. three times daily for 7 days. They performed daily darkfield examinations for *Treponema pallidum* and saw actively motile treponemes on each occasion, although the organisms were more difficult to find on the fifth and sixth days of treatment. On the seventh day there was no evidence of healing and darkfield examination showed one to four actively motile *Treponema pallida* per $\frac{1}{12}$" field.

Thus, as far as it goes, the available evidence is reassuring, for it suggests that in the dosage usually prescribed metronidazole has only a slight effect upon *Treponema pallidum*. Nevertheless, the data are far from comprehensive and doubts remain as to the possible effects of this drug on syphilis in the incubation period and in some cases of early clinical disease. The fact of this uncertainty calls for closer investigation on a wider scale. In the meantime there is a case for temporarily withholding the drug in cases where infection with syphilis within the incubation period is a considerable possibility.

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